

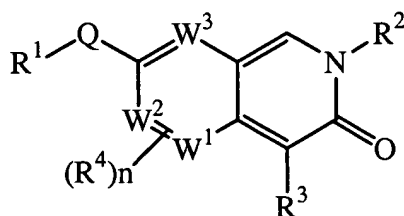
AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of claims:

Claim 1 (currently amended).

A compound of Formula I



I

or a pharmaceutically acceptable salt thereof,
wherein:

R¹ is independently selected from:

- C₅ or C₆ cycloalkyl-(C₁-C₈ alkylenyl);
- Substituted C₅ or C₆ cycloalkyl-(C₁-C₈ alkylenyl);
- C₈-C₁₀ bicycloalkyl-(C₁-C₈ alkylenyl);
- Substituted C₈-C₁₀ bicycloalkyl-(C₁-C₈ alkylenyl);
- 5- or 6-membered heterocycloalkyl-(C₁-C₈ alkylenyl);
- Substituted 5- or 6-membered heterocycloalkyl-(C₁-C₈ alkylenyl);
- 8- to 10-membered heterobicycloalkyl-(C₁-C₈ alkylenyl);
- Substituted 8- to 10-membered heterobicycloalkyl-(C₁-C₈ alkylenyl);
- Phenyl-(C₁-C₈ alkylenyl);
- Substituted phenyl-(C₁-C₈ alkylenyl);
- Naphthyl-(C₁-C₈ alkylenyl);
- Substituted naphthyl-(C₁-C₈ alkylenyl);
- 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
- Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
- 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl); and
- Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);

Phenyl;
Substituted phenyl;
Naphthyl;
Substituted naphthyl;
5- or 6-membered heteroaryl;
Substituted 5- or 6-membered heteroaryl;
8- to 10-membered heterobiaryl;
Substituted 8- to 10-membered heterobiaryl;

R² is independently selected from:

H;
C₁-C₆ alkyl;
Phenyl-(C₁-C₈ alkylenyl);
Substituted phenyl-(C₁-C₈ alkylenyl);
Naphthyl-(C₁-C₈ alkylenyl);
Substituted naphthyl-(C₁-C₈ alkylenyl);
5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl); and
Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);
Phenyl-O-(C₁-C₈ alkylenyl);
Substituted phenyl-O-(C₁-C₈ alkylenyl);
Phenyl-S-(C₁-C₈ alkylenyl);
Substituted phenyl-S-(C₁-C₈ alkylenyl);
Phenyl-S(O)-(C₁-C₈ alkylenyl);
Substituted phenyl-S(O)-(C₁-C₈ alkylenyl);
Phenyl-S(O)₂-(C₁-C₈ alkylenyl);
Substituted phenyl-S(O)₂-(C₁-C₈ alkylenyl);

Each substituted R¹ and R² group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C₁-C₆ alkyl;
CN;

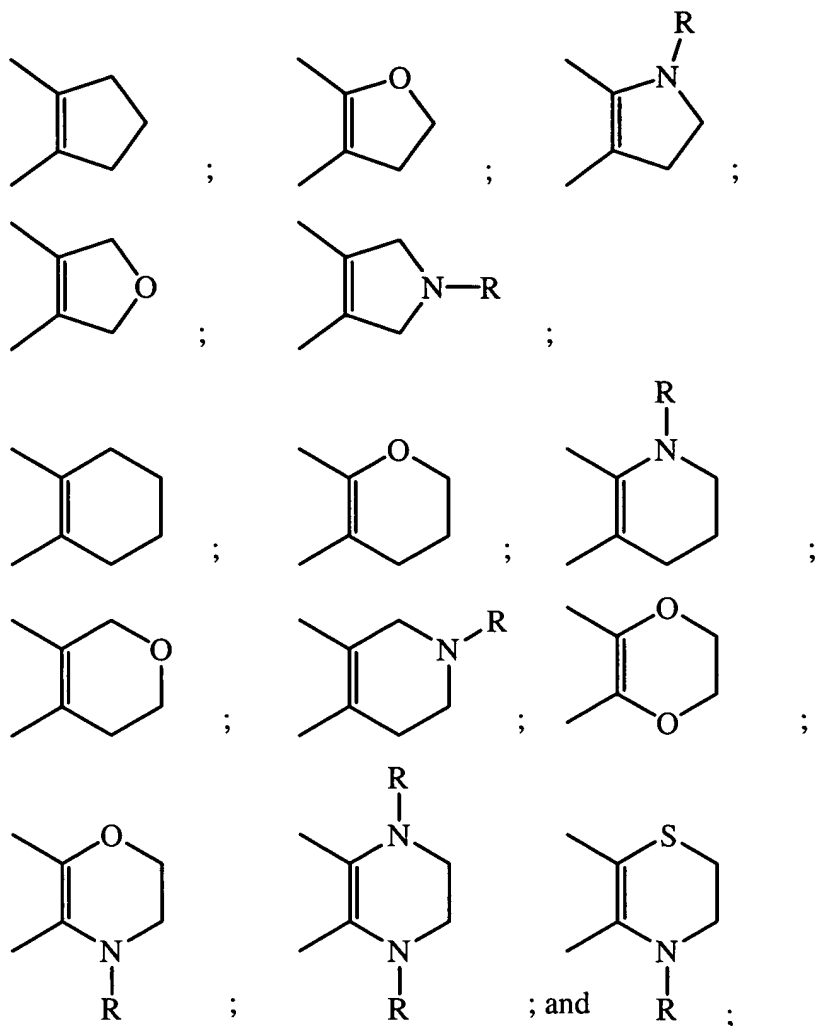
CF_3 ;
 HO ;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-O}$;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-S(O)}_2$;
 H_2N ;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-N(H)}$;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})_2\text{-N}$;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-C(O)O-(C}_1\text{-C}_8 \text{ alkylenyl})_m$;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-C(O)O-(1- to 8-membered heteroalkylenyl)}_m$;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-C(O)N(H)-(C}_1\text{-C}_8 \text{ alkylenyl})_m$;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-C(O)N(H)-(1- to 8-membered heteroalkylenyl)}_m$;
 $\text{H}_2\text{NS(O)}_2\text{-(C}_1\text{-C}_8 \text{ alkylenyl)}$;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-N(H)S(O)}_2\text{-(C}_1\text{-C}_8 \text{ alkylenyl})_m$;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})_2\text{-NS(O)}_2\text{-(C}_1\text{-C}_8 \text{ alkylenyl})_m$;
3- to 6-membered heterocycloalkyl-(G)_m;
Substituted 3- to 6-membered heterocycloalkyl-(G)_m;
5- or 6-membered heteroaryl-(G)_m; and
Substituted 5- or 6-membered heteroaryl-(G)_m;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-S(O)}_2\text{-N(H)-C(O)-(C}_1\text{-C}_8 \text{ alkylenyl})_m$;
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-C(O)-N(H)-S(O)}_2\text{-(C}_1\text{-C}_8 \text{ alkylenyl})_m$;

wherein each substituent on a carbon atom may further be independently selected from:

Halo ; and
 HO_2C ;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O ;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:



R is H or C₁-C₆ alkyl;

G is CH₂; O, S, S(O); or S(O)₂;

Each m is an integer of 0 or 1;

R³ is selected from the groups:

H;

C₁-C₆ alkyl;

Substituted C₁-C₆ alkyl;

C₂-C₆ alkenyl;

Substituted C₂-C₆ alkenyl;

C₂-C₆ alkynyl;

Substituted C₂-C₆ alkynyl;

C₃-C₆ cycloalkyl;

Substituted C₃-C₆ cycloalkyl;
C₃-C₆ cycloalkyl-(C₁-C₈ alkylenyl);
Substituted C₃-C₆ cycloalkyl-(C₁-C₈ alkylenyl);
Phenyl;
Substituted phenyl;
Phenyl-(C₁-C₈ alkylenyl);
Substituted phenyl-(C₁-C₈ alkylenyl);
Naphthyl;
Substituted Naphthyl;
Naphthyl-(C₁-C₈ alkylenyl);
Substituted naphthyl-(C₁-C₈ alkylenyl);
3- to 6-membered heterocycloalkyl;
Substituted 3- to 6-membered heterocycloalkyl;
3- to 6-membered heterocycloalkyl-(C₁-C₈ alkylenyl);
Substituted 3- to 6-membered heterocycloalkyl-(C₁-C₈ alkylenyl)
HO;
(C₁-C₆ alkyl)-O;
H₂N;
(C₁-C₆ alkyl)-N(H);
(C₁-C₆ alkyl)₂-N;

Each substituted R³ group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

H₂N;
C₁-C₆ alkyl;
CN;
CF₃;
(C₁-C₆ alkyl)-OC(O);
HO;
(C₁-C₆ alkyl)-O;
HS; and
(C₁-C₆ alkyl)-S;

wherein each substituent on a carbon atom may further be independently selected from:

Halo; and

HO₂C;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

R⁴ is H, C₁-C₆ alkyl, H₂N, HO, or halo;

n is an integer of from 0 to 3;

Q is selected from:

OC(O);

CH(R⁵)C(O);

OC(NR⁵);

CH(R⁵)C(NR⁵);

N(R⁵)C(O);

N(R⁵)C(S);

N(R⁵)C(NR⁵);

N(R⁵)CH₂;

SC(O);

CH(R⁵)C(S);

SC(NR⁵);

trans-(H)C=C(H);

cis-(H)C=C(H);

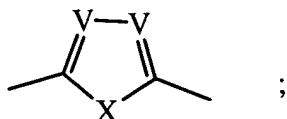
C≡C;

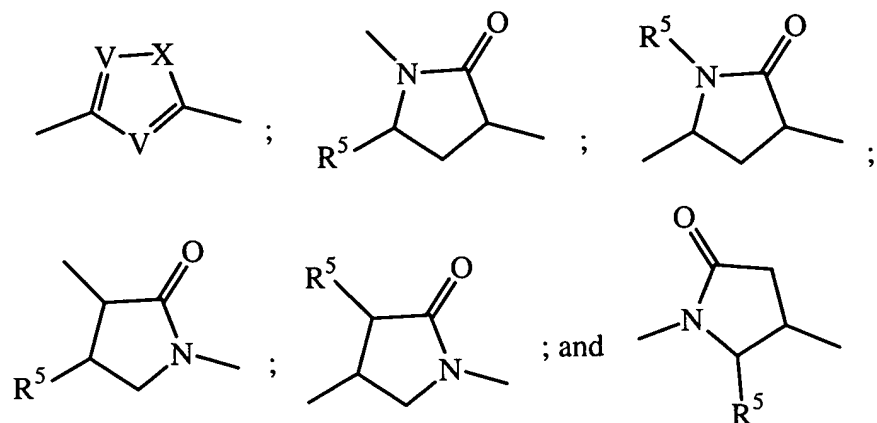
CH₂C≡C;

C≡CCH₂;

CF₂C≡C; and

C≡CCF₂;





R⁵ is H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl; 3- to 6-membered heterocycloalkyl; phenyl;

benzyl; or 5- or 6-membered heteroaryl;

X is O, S, N(H), or N(C₁-C₆ alkyl);

Each V is independently C(H) or N;

~~Each W¹, W², and W³ is independently N or C-R⁴, wherein R⁴ is as defined above;~~

One of W¹, W², and W³ is N and the other two of W¹, W², and W³ are each C-R⁴,
wherein R⁴ is as defined above;

wherein each C₈-C₁₀ bicycloalkyl is a bicyclic carbocyclic ring that contains 8-, 9-, or 10-member carbon atoms which are 5,5-fused, 6,5-fused, or 6,6-fused bicyclic rings, respectively, and wherein the ring is saturated or optionally contains one carbon-carbon double bond;

wherein each 8- to 10-membered heterobicycloalkyl is a bicyclic ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond, and wherein the heterobicycloalkyl is a 5,5-fused, 6,5-fused, or 6,6-fused bicyclic ring, respectively,

wherein each heterocycloalkyl is a ring that contains carbon atoms and from 1 to 4 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 4 N(H), and 4 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded

to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C₁-C₆ alkyl), and 5- and 6-membered heteroaryl are monocyclic rings;

wherein each heterobiaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and where the 8-, 9-, and 10-membered heterobiaryl are 5,5-fused, 6,5-fused, and 6,6-fused bicyclic rings, respectively, and wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;

wherein with any (C₁-C₆ alkyl)₂-N group, the C₁-C₆ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and

wherein each group and each substituent recited above is independently selected.

Claims 2 and 3 (cancelled).

Claim 4 (original). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is N(R⁵)C(O) or C≡C.

Claim 5 (original). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein Q is C≡C.

Claim 6 (original). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein n is 0.

Claim 7 (original). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein n is 1.

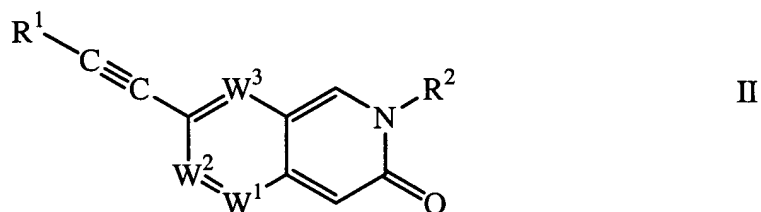
Claim 8 (currently amended). The compound according to any one of ~~Claims 1 to 7~~ Claims 1 or 4 to 7 inclusive, or a pharmaceutically acceptable salt thereof, wherein R¹ is independently selected from:

- 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
- Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
- 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);
- Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);
- Phenyl-(C₁-C₈ alkylenyl); and
- Substituted phenyl-(C₁-C₈ alkylenyl); and

R² is independently selected from:

- 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
 - Substituted 5- or 6-membered heteroaryl-(C₁-C₈ alkylenyl);
 - 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);
 - Substituted 8- to 10-membered heterobiaryl-(C₁-C₈ alkylenyl);
 - Phenyl-(C₁-C₈ alkylenyl); and
 - Substituted phenyl-(C₁-C₈ alkylenyl);
- wherein each group and each substituent is independently selected.

Claim 9 (original). The compound of Claim 1 of Formula II



or a pharmaceutically acceptable salt thereof.

Claim 10 (cancelled).

Claim 11 (original). A pharmaceutical composition, comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

Claim 12 (cancelled).

Claim 13 (original). A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis a nontoxic effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof.

Claim 14 (cancelled).

Claim 15 (new). The compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein W^2 is N and W^1 and W^3 are each C- R^4 , wherein R^4 is as defined above.